REMARKS

This paper is submitted for consideration in response to the non-final Office Action mailed on April 11, 2007. Claims 1-25 are pending. Claims 4-6, 18, and 22 are withdrawn due to restriction. Claims 1-3, 7-17, 19-21, and 23-25 are under examination. Applicants respectfully request consideration and entry of the amendments and remarks contained herein. No new matter has been added.

Claim 1 is amended to clarify that the polynucleotides are attached to the substrate surface via the trityl linker when the matrix material is applied to the polynucleotides on the substrate meaning that there is **no cleavage** or step to produce cleavage of the polynucleotide from the substrate nor enzymatic degradation of the polynucleotide ***prior*** exposing the substrate and the ***bound polynucleotide to the substrate*** to the matrix and laser, in other words the substrate with the full length embedded polynucleotides and with the applied matrix material are placed into the MALDI source, e.g., into the apparatus, and subjected to MALDI analysis. Similar amendments are also made in claim 12. Support for the amendments is found throughout the specification, including page 27, lines 5-7 and page 28, lines 21-23.

35 USC § 102

Claims 1-3, 7-14, 19-21, and 23-25 are rejected under 35 USC § 102(b) as being anticipated in view of Guerlavais et al., *Analytical and Bioanalytical Chemistry,* 374:57-63 (2002). Applicants respectfully traverse.

Claim 1 is directed to a method of analyzing a polynucleotide using MALDI where the polynucleotide is bound to a substrate *via a triaryl methyl linker* and the polynucleotide bound to the substrate is contacted with matrix material *on the substrate* and subsequently the substrate/polynucleotides/matrix is subjected to MALDI.

For anticipation under 35 U.S.C. §102, each and every element as set forth in the claim must be described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California,* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The anticipation rejection asserts that Guerlavais which teaches the use of MALDI to characterize solid supported oligonucleotides and that certain disclosed chemistries of Guerlavais, namely, "5-O-Dimethoxytrityl-1,2-dideoxyribose-3-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite" at page 58 meets the requirements of claims 1, 10, 17, 19, and 20.

However, Applicants disagree with the assertions of the rejection. For example, the chemistries disclosed on page 58 and figure 2 on page 59 of Guerlavais, reproduced below, do not meet the claimed chemistries.

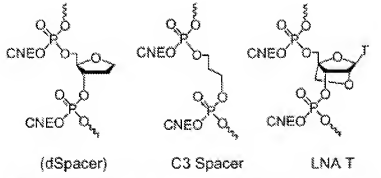

Fig. 2 Chemical structures of dSpacer, C3 Spacer, and LNA T in po-CNE ON

The full description at page 58 is "5-O-Dimethoxytrityl-1,2-dideoxyribose-3-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite (dSpacer phosphoramidite)." The dSpacer is shown in Figure 2 of page 59 (above). The dSpacer, and other suggested linkers, do not include trityl groups.

In contrast to the claimed methods, the methods of Guerlavais require non-trityl linkers. This is because Guerlavais uses trityl as a protecting group on the 5' position of each nucleotide added to the growing chain. Because trityl is used as protecting group, it cannot be also used as a linker -- otherwise each time the substrate surface is subjected to acid treatment to remove the trityl protecting group during addition of the next nucleotide, the growing chain would simply be cleaved from the substrate surface. This is an inoperative result. Consequently, the linkers disclosed by Guerlavais are all photosensitive linkers. The photosensitive linkers are used because they are required to be able to withstand the standard phosphoramidite chemistries used for oligonucleotide synthesis employed in Guerlavais. *See* page 58, 1st paragraph of Results and

Discussion. Consequently, Guerlavais does not meet the requirement for a trityl linker presented in the pending claims. Withdrawal of the rejection of the claims in view of Guerlavais is respectfully requested.

35 USC § 102(b) - Koster:

Claims 1-3, 7-17, 19-21, and 23-25 are rejected under 35 USC § 102(b) as being anticipated by Koster et al., U.S. Patent No. 6,074,823. Applicants respectfully traverse.

For anticipation under 35 U.S.C. §102, each and every element as set forth in the claim must be described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

As above-indicated, claim 1 requires an oligonucleotide attached to a substrate via a triaryl methyl linker group and that nucleotide to be attached to a substrate surface when contacted with the matrix material and subsequently the substrate/ oligonucleotide matrix to be subjected to MALDI.

As admitted by the Office, Koster teaches mass spectrometry based processes requiring oligonucleotide degradation via exonuclease digestion, where the degraded pieces are then collected, prepared for mass spec and then detected by mass spec using MALDI. Koster does not teach or suggest that **un-degraded** oligonucleotides immobilized on a support be subjected directly to MALDI. In fact, Koster repeatedly describes the removal of oligonucleotides from the solid support and their subsequent enzymatic degradation prior to application of the matrix and subjection of the nucleotide fragments to mass spec. Therefore, Koster does not teach all the limitations of the pending claims. Withdrawal of the rejection in view of Koster is respectfully requested.

SUMMARY

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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Date: August 9, 2007

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